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MARSCHEL, A

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MR. WILLIAN NEEDLE
NEEDLE AND ROSENBERG
THE CARGNEGIE BLDG., SUITE 400
133 CARNEGIE WAY
ATLANTA, GA 30303

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 12-4-92 and 12-31-92 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 44-47 and 60 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☒ Claims 1-43 and 48-59 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 44-47 and 60 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

Applicants' arguments filed 12/4/92 and 12/31/92 have been fully considered and they are deemed to be persuasive to overcome the rejections as previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are newly applied to the claims as stated. They constitute the complete set presently being applied to the instant application.

As a result of rejections newly applied to the present claims the FINAL REJECTION status of the instant application is hereby withdrawn.

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 44-47 and 60 are rejected under 35 U.S.C. § 101 because they lack of cited and claim utility of diagnosing or evaluating the presence of cancer in a human. Upon an extensive review of the supporting evidence the Examiner has not found persuasive evidence for cancer diagnostic or indicative utility for the instant invention. The results directed to in-vitro cell line methods are not further supported by significant evidence of patient in-vivo utility. It is well known in the art that the correlation of in-vitro results to in-vivo results requires clear evidence especially in the well known unpredictable art of cancer evaluation or diagnosis. Each of the references supplied by applicants are responded to as follows:

Varmus

Firstly, Varmus is cited regarding the NIH3T3 cell test system. The Examiner has not found any support therein for wide acceptance of this system. In fact, on page 559, lines 18-36, the NIH3T3 system is cited as stimulating advances in understanding but failing to observe transforming activity in 80-90% of tumors. Varmus then goes on to discuss the investigation of other cells lines clearly motivated by said failure of the NIH3T3 system.

Bargmann et al.; Cell 45:649 (1986) and Muller et al.

Rat and transgenic oncogene results are discussed without any evidence as to its applicability to human oncogene activation etc. No correlations to human tumors are studied even as minimal evidence.

De Fiore et al. and Hudziak et al.

The results given both in De Fiore et al. and Hudziak et al. are directed to the NIH3T3 system. Since applicants have cited this in support of utility, assertions therein as to utility are insufficient. The evidence therein supplied only goes to a study of NIH3T3 cells which has already been discussed above as seriously failing regarding cancer studies.

Paik et al. and Lacroix et al.

These references have been already discussed relative to being non-persuasive regarding this issue in the office action mailed 6/2/92.

Iglehart et al.

Table I on page 6703 and Table 2 on page 6704 cite tumor studies but do not disclose controls. Without clear control disclosure to contrast results, the evidence of diagnostic utility is lacking.

Yokota et al.

On page 766, second column, first paragraph, amplification of c-erb-2 is cited as observable in 5 of 63 adenocarcinomas. This is hardly persuasive of significant correlation.

Zhou et al.

In the abstract an increased frequency of amplification in tumors is described but only as an increased frequency and without concluding diagnostic utility. On page 6125, second column, last sentence of the last paragraph, Zhou et al. suggests that alterations in c-erb-2 should be examined in breast cancer cases. Such suggestion for further research is clearly defined in the M.P.E.P. § 608.01(p) entitled 35 U.S.C. 101 as insufficient for supporting utility which must be present in current and available form.

Varley et al.

Varley et al. discusses the neu oncogene amplification on page 428, second column, line 30, through page 429, first column, line 6. Only 19% of their carcinoma samples showed neu amplification. Apparently Varley et al. remained unconvinced as to the diagnostic utility of this finding since on page 429, first 6 lines, they state that disturbance of neu sequences may result in clinical phenotype and experiments are in progress to

address this proposal.

Press et al.

Press et al. summarize in the abstract that normal tissues including fetal tissue express neu mRNA and such expression is also found in non-overexpressing breast cancers again without a conclusion of diagnostic utility. On page 960, second column, lines 14-28, only potential utility in diagnostic and prognostic tests is disclosed. Press et al. also states that therapeutic approaches will most likely be based on differential high levels of expression. These are clear non-conclusionary statements that further document the further research needed to support utility.

In summary, the evidence supplied by applicants as to the cancer utility of the instant invention is tantilizing and certainly suggestive that such utility may exist. The Examiner would also like to point out that applicants have not clearly defined what art recognized standard must be satisfied for diagnostic cancer utility. Is there a correlation threshold etc? For the above cited reasons further research is clearly indicated before said cancer utility is shown in currently available form and this clearly documents the lack of utility that is sufficient for the purposes of 35 U.S.C. § 101.

Claims 44-47 and 60 are allowable over the prior art of record because the particular polynucleotide compositions are neither taught nor suggested by the prior art of record.

No claim is allowed.

Papers related to this application may be submitted to Group

180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

The CM1 Fax Center number is (703) 308-4227.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

AM

A. MARSCHEL:am

February 8, 1993

CHRISTINE M. NUCKER
SUPERVISORY PATENT EXAMINER
GROUP 180